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EXAMINER	
FOSTER, CHRISTINE E	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,006	KARL ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-52,73 and 74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-52,73 and 74* is/are rejected.

7)☒ Claim(s) *44-45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/20/06 has been entered.

Claims 70-72 have been canceled.

New claims 73-74 have been added

Claims 44-52 and 73-74 are currently pending.

Rejections Withdrawn

2. The rejections of claims 44-48 under 35 USC 112, 1st paragraph for written description (new matter) set forth in the previous Office action are withdrawn in response to Applicant's amendments to recite "separately determining" rather than a signal generating group "bound separately". However, the amended claims have presented new grounds of rejection under this statute set forth below.

3. The rejections of claims 49 and 51 under 35 USC 102(b) as being anticipated by Bellet et al., and of claims 50 and 52 under 35 USC 103(a) as being unpatentable over Bellet al. in view of Kuo, are withdrawn in response to Applicant's amendments, in particular due to the amendment to claim 49 to recite that an analyte bound to the first test area is not simultaneously bound to the second test area.

4. The rejections of claims 45-46 and 50 under 35 USC 103(a) as being unpatentable over Linsley et al. in view of Mehta, and of claims 46, 48, 50 and 52 as being unpatentable over Linsley et al. in view of Valkirs et al. are upon further consideration by the Examiner.

Information Disclosure Statement

Applicant's Information Disclosure Statement filed 9/16/05 has been received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449. Citation Nos. 1-4 have been lined through because the references are already of record.

Claim Objections

5. Claim 45 objected to because of the following informalities: the claim refers to "HIVI" which should appear as "HIV I" (or "HIV-I"). In addition, it is suggested that at the first instance of the abbreviations HIV, HBV, and HCV in the claims that the abbreviations be accompanied by the full term.

6. Claim 44 now recites "**at least** a first and second receptor" in part (a). Part (b) refers to "**one or more** third receptors". The use of the descriptions "first", "second" and "third" is confusing now that there may be more than three receptors employed in the method.

7. Claim 44 has a typographical error in that the word "wherein" is misspelled in line 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 44-52 and 73-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

10. Amended claims 44, 49, and 51 recite a method for simultaneous, separate "**multicomponent**" detection of an analyte in a sample which represents a departure from the specification and claims as originally filed. The claims have also been amended to recite that the analyte comprises at least two **analyte-specific components**. Claims 44 and 49 now recite that the first and second receptors bind to different **analyte-specific** components of the analyte and that the first and second receptors bind to different **components** of the analyte and that the *first receptor binds via a first analyte-specific component* and the *second receptor binds via a second analyte-specific component*. New claim 73 also refers to **analyte-specific components.**

It is noted that Applicant is apparently employing the term "analyte" to refer not only to a single molecule but also to a heterogeneous antibody population, an antigen mixture, or a mixture of antigens and antibodies that may be different (as in claim 73; see rejection under 112, 2nd paragraph below).

Applicant states that support for the above amendments may be found in the specification at p. 5, 4th paragraph -- page 6, 3rd paragraph and in the Examples, especially Example 1. However, no support could be found for the limitations of **multicomponent** detection, of

analytes that comprise multiple "**analyte-specific components**", or of receptors binding to different **analyte-specific components**. These terms are not disclosed or defined in the specification. The specification indicates that in the case of a homogeneous analyte population, the analyte receptors may bind to different epitopes of an analyte (such as an antigen) (see p. 5, the last two lines to page 6, line 5). The specification further discloses that alternatively, the receptors may bind to different analyte subtypes such as antigen subtypes, and/or to different analyte types such as different antigens and/or antibodies.

The above disclosure of analytes having different epitopes, and of heterogeneous mixtures of antibodies, antigens, or antigen-antibody mixtures fails to provide support for the genus of analytes having multiple components as now claimed.

The term "**components**" as regards such an analyte is not defined in the specification. Given the broadest reasonable interpretation of this term, however, "component" has a meaning that is broader in scope that the species of antigens, antibodies, and epitopes that are disclosed. For example, the "components" of an analyte are not restricted to antigens, antibodies, or antigen-antibody mixtures, but could refer to moieties that are neither antigens nor antibodies, such as carbohydrate structures or lipids on a protein, or nucleic acids. Applicant is therefore effectively claiming a new genus of analytes having multiple "components", as well as receptors binding to different such "components" that is not supported by the specific disclosure of a mixture of antigens, antibodies, and antigen-antibody mixtures.

11. Amended claim 49 recites the limitation that "**an analyte bound to the first test area is not simultaneously bound to the second test area**", which represents a departure from the specification and claims as originally filed. Any negative limitation or exclusionary proviso must

have basis in the original disclosure (see MPEP 2173.05(i)). There is also no indication in the specification that this feature is inherently necessarily and always present in the claimed invention.

Applicant indicates that support for this amendment may be found in Examples 2-3. However, no support could be found for such a limitation where indicated. Examples 2-3 relate to detection of HIV antibodies and antigens. It is noted that Applicant is broadly employing the term "analyte" in the claims, such that "an analyte" encompasses not only to a single molecule (such as a particular HIV antigen) but may also refer to heterogeneous mixtures of "at least two different analyte-specific antigens," "at least two different analyte-specific antibodies," or "at least one analyte-specific antigen and one analyte-specific antibody" as recited in claim 73. In this light, the "analyte" of Examples 2-3 is "HIV". The multiple "analyte-specific components" of the HIV analyte that are detected in the Examples are the monoclonal antibodies specific for HIV (different analyte-specific antibodies) and HIV peptide antigens (different analyte-specific antigens).

No support could be found for recited limitation that the analyte may not simultaneously be found to both the first and second test areas in Examples 2-3. To the contrary, the data of Examples 2-3 show that the analyte (HIV) was detected in more than one test area, as more than one test areas were occupied by the various different analyte-specific components (see the Tables on p. 25 and 27). For example, components of HIV were detected in the p24 test area as well as the gp41 peptide 1 and gp41 peptide 2 test areas (see the Table of p. 25, the line corresponding to patient R, 4^{th} withdrawal). Therefore, at the time of this 4^{th} withdrawal, the analyte HIV was simultaneously bound to more than one test area. In consequence, no support could be found for

an analyte bound that is bound to the first test area and not simultaneously bound to the second test area, in particular due to the manner in which Applicant is employing the terms "analyte" and "analyte-specific components" in the claims.

12. Claims 48 and 52 have been amended to recite that the detection reagent comprises a **"signal-generating reagent"**, which represents a departure from the specification and claims as originally filed. Applicant indicates that support may be found at page 5, lines 7-10, at which the specification discloses an analyte-specific receptor that "carries a signal generating group or is capable of binding to a signal generating group". However, no support could be found for a detection reagent comprising "signal-generating reagent" where indicated by Applicant. The term "signal-generation reagent" is not disclosed.

Furthermore, claim 44 recites a detection reagent that comprises one or more third receptors that are bound to a signal-generating group. The specification passage above indicates that the signal-generating group is bound (or can bind) to the free (third) receptor. However, the "signal-generating reagent" that is recited in claims 48 and 52 is not recited as being bound to the one or more third receptors; it could be provided as a separate ingredient included in the detection reagent composition. There is no disclosure of signal-generating groups (or reagents) that are not bound or capable of binding to the free third receptor.

13. New claim 74 recites that the presence or amount of the analyte is determined via a "test area-specific cut-off". Applicant indicated that support may be found for the amendment at p. 10-11. At p. 11, the first full paragraph, the specification discloses:

> "*If several test areas are used which each allow the determination of different analyte molecules*, it has often proven to be expedient to define a test area specific cut-off value" (emphasis added)

The new claim represents new matter because there is no generic disclosure of the use of a test area-specific cut-off value. Rather, the above passage discloses such a value for embodiments when different analyte molecules are being determined. However, claim 74 does not recite the accompanying limitation that different analyte molecules are being determined. The claims currently encompass not only determination of different analyte molecules (e.g., as in claim 73), but also determination of a single analyte molecule having multiple epitopes. No support could be found for the use of a test area-specific cut-off value when a single analyte molecule is being determined.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 44-52 and 73-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "**analyte**" in claims 44-52 and 73-74 is apparently used by the claim to mean "**a heterogeneous population of different molecules**", while the accepted meaning is "**a single molecule.**" The term is indefinite because the specification does not clearly redefine the term.

Amended claims 44, 49, and 51 recite "multicomponent" detection of "**an analyte**." The recitation of "an analyte" implies that a single species is being detected. Claim 45 also refers to "the analyte". However, new claim 73 recites that the analyte may comprise "two different...antigens, two different..antibodies or at least one...antigen and one...antibody."

The specification does not clearly define the term "analyte". The specification at p. 5, the last paragraph suggests that the analyte may be a homogeneous or heterogeneous population. However, this exemplification does not represent a limiting definition of the term "analyte".

An "analyte" has been defined as "**a molecule** that is targeted by a particular quantification method" (Macmillan Dictionary of Toxicology (1999). Retrieved 16 May 2006, from xreferplus. http://www.xreferplus.com/entry/972936, emphasis added). In this light, it is clear that one skilled in the art would understand the term "analyte" to refer to a single molecule or species that is detected.

Since the term "analyte" is currently being used by Applicant in a broader sense that is contrary to its ordinary meaning, and because the term is not clearly redefined in the specification, one skilled in the art would not be reasonably apprised of the metes and bounds of the term "analyte".

17. Claims 44, 49, and 51 recite the limitation "**multicomponent**", which is vague and indefinite. The term is not defined in the specification, such that one skilled in the art would not be reasonably apprised of the metes and bounds of the term "multicomponent".

18. Claims 44, 49, 51, and 73-74 refer to "**analyte-specific components**". Claim 49 also refers to "**components**" of an analyte. The terms are vague and indefinite. The terms are not

defined in the specification, such that one skilled in the art would not be reasonably apprised of the metes and bounds of "analyte-specific components" or "components" of an analyte.

19. Claim 74 recites the limitation "the signal generating group bound to the first and second test areas via **the at least two analyte-specific components**". There is insufficient antecedent basis for this limitation in the claims. Claim 44 refers to "the signal generating group bound to the first and second test areas via **said analyte**".

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 44, 47, 49, 51, and 74 are rejected under 35 U.S.C. 102(e) as being anticipated by Linsley et al. (US Patent No. 6,004,761, filed June 2, 1995).

Linsley et al. teach double determinant immunoassay (DDIA) methods wherein a capture antibody is immobilized on a solid phase such as a plastic support or polystyrene microtiter plate, in order to detect an antigen present in a fluid sample (column 4, lines 6-30; column 13, lines 2-4 in particular). Following capture of the antigen by the immobilized antibody, a labeled antibody is added which may bind to a different epitope on the captured antigen than the immobilized antibody (column 4, lines 11-17 and 21-30; Examples IV, VII, and IX; and Tables 5 and 12 in particular). In particular, Linsley et al. teach immobilization of multiple antibodies that are specific for different epitopes of the mucin antigen (see in particular column 2, lines 56-63;

Example IV; and columns 24 to column 25, line 44), wherein each type of antibody is bound to a spatially separate test area, i.e. a different well of a microtiter plate (column 17, lines 57-60 in particular).

The solid phase (Immulon II microtiter plates; see also column 13, lines 2-5) comprises a non-porous support (polystyrene) and includes first and second spatially separate test areas (wells). It would be immediately apparent to one of skill in the art that microtiter plates comprise an inert surface between the wells that does not bind to the analyte or other sample components. Linsley et al. teach first and second receptors (the antibodies Onc-M26 and Onc-M29) that bind to different components (epitopes) of the analyte (mucin antigen) (see column 4, lines 6-30; column 17, lines 11-31). In Example IV, Linsley et al. teach that each of these antibodies was coated onto a different well of the solid phase (column 17, line 49 to column 18, line 54).

The sample (diluted sera, control or standard) is contacted with the solid phase and with a detection reagent comprising a third receptor (W1-HRP conjugated antibody) that binds with the antigen (see column 2, lines 10-11) and that is bound directly (conjugated) to a signal generating group (HRP), and the presence of amount of the signal generating group is determined for each well in order to determine the amount of antigen in the sample (see column 18, lines 18-41; Table 5; column 19, lines 14-26; and column 25, lines 46-64; and column 4, lines 15-18 in particular). The signal generating group is "separately" determined since data are reported for each well (Table 5).

With regard to claim 47, serum from a patient without cancer is added to some of the wells as a control (see for example column 4, lines 10-11; column 17, line 65 to column 18, line 19).

With regard to claim 49, the analyte (mucin antigen) bound to wells having Onc-M26 immobilized as well as to wells having Onc-M29 immobilized; however, Linsley et al. anticipates this limitation since a single molecule of mucin antigen would not be simultaneously bound to multiple wells due to the physical separation between wells as a result of the structure of the microtiter plate.

With regard to claim 51, Example IV of Linsley et al. teaches the solid phase discussed above as well as the detection reagent discussed above, which is a third analyte-specific receptor (W1-HRP conjugated antibody) bound to the signal-generating group HRP. Diagnostic test kits for detection of mucin antigens in serum or other specimens are also taught (column 30, line 55 to column 31, line 32).

With regard to claim 74, Linsley et al. teach test area-specific cut-off values (see in particular Table 5; column 18, lines 38-41).

22. Claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Fleming (US 5,149,626).

Fleming teaches a solid phase comprising a non-porous support such as microtiter plates, glass, polystyrene, or polypropylene (see the abstract; column 5, lines 11-21 and 63-68; column 8, lines 40-68). The solid phase contains one or more different antigen-specific receptors (antibodies) that are separately immobilized to separate, defined areas on the solid phase (Figure 1; column 3, line 40 to column 4, line 30).

Fleming teaches that the solid phase may be used to detect multiple antigens or analytes in a sample (see also column 7, line 35 to column 8, line 3). An analyte may include proteins or

viruses (column 5, lines 38-43). The teaching of different antigen-specific antibodies to assay for multiple antigens in a sample anticipates the limitation of receptors binding to an analyte via different components of the analyte, in that the different antigens represent different "components" of the sample. The sample containing multiple antigens and the different antigen-specific antibodies taught by Fleming anticipate the first and second receptors that bind to different "analyte-specific components" as claimed because Applicant has not specifically defined the terms "analyte" or "analyte-specific component", and further because Applicant is employing the term "analyte" broadly such that it may refer not only to a single molecule but also to a mixture of multiple antigens in a sample, as in claim 73. Thus, the mixture of different antigens taught by Fleming reads on the claimed analyte and the antibodies specific for different antigens in the sample reads on the claimed first and second receptors binding to different "analyte-specific components".

The recitation that "an analyte bound to the first test area is not simultaneously bound to the second test area" refers to the intended use of the claimed solid phase and has not been given patentable weight in construing the claims. If a prior art structure is capable of performing the intended use as recited in the preamble, then it meets the claim. See, e.g., In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). In the instant case, the solid phase of Fleming includes antibodies immobilized in different test areas that are specific for different antigens, and may be used in a method to detect an analyte sample having different antigens. In such a case, an antigen bound via a specific antibody to a first defined area would not be bound to a second defined area bearing an antibody that is specific for a different antigen.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 44-46, 48-52 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. (US 5,516,635) in view of Schonbrunner (UK Patent Application Publication GB 2313 666 A).

Ekins et al. teach a solid phase ("solid support"), kit, and a method of using same that includes multiple test areas "microspots" on which capture binding agents such as antibodies may be immobilized (column 2, lines 6-16 and 56-60; column 5, lines 10-59). The solid phase may comprise a non-porous support (plastic or polystyrene microtitre plate; see column 7, lines 59-60; Examples 5-6). Such a support comprises an inert surface between the test areas (wells) that does not bind to the analyte or other sample components (i.e., the partitions that separate the wells of the microtiter plate), which would be immediately apparent to one skilled in the art. More generally, the areas between the microspots on the solid support would constitute such an inert surface since no immobilized material is spotted between the spots; since there are no reagents available for binding in the regions between the microspots such regions would not bind to the analyte or sample components.

Ekins et al. further teach a detection reagent comprising a receptor ("developing binding material") that also binds with the analyte and is labeled with a signal-generating group, such as by adsorption or covalent binding to a latex microsphere carrying a fluorescent or enzyme label (see the abstract; column 1, lines 53-65; columns 3-5). Thus, Ekins et al. teach a first analyte-specific receptor immobilized on a first test area, as well as a detection reagent comprising a receptor that binds specifically with the analyte and that is bound to a signal-generating group. The solid phase may be combined together with the detection reagent in a kit (column 10, lines 17-58; and column 10, claims 15-16).

Ekins et al. further teach that the solid phase may be used in a method to simultaneously determine multiple analytes in the same sample by immobilizing different receptors on different microspots (column 10, lines 52-58; column 18, claim 6). Either the same or detection reagents

could be used in separate determinations for each microspot ("different binding assays") (see column 5, lines 28-40; column 9, line 61 to column 10, line 4). The method includes the steps of contacting a liquid sample containing an analyte with at least two "analyte-specific components" ("binding sites") (column 1, lines 12-55; column 8, lines 14-58) with the solid phase containing an immobilized receptor that binds to the analyte via an analyte-specific component (column 9, lines 37-57; claims 1-14; and Examples 5-12 in particular). The analyte may be nucleic acid, hormones, viruses, proteins, etc. (column 8, lines 17-38).

Ekins et al. fail to specifically teach that the different receptors immobilized on different test areas (microspots) are specific for different "analyte-specific components" of the same "analyte". Although Ekins et al. teach multiple receptors specific for different analyte-specific components of an analyte, only one of the receptors is immobilized and the other is used as the detection reagent.

Schonbrunner teaches an assay method for simultaneously detecting HIV antigens and HIV antibodies (the abstract; p. 1, lines 1-4;). Note that due to the manner in which the terms "analyte" and "analyte-specific component" are being employed in the claims, the "analyte" in the method of Schonbrunner is HIV, while HIV antigens and HIV antibodies are each "analyte-specific components". Schonbrunner teach that detecting both HIV antigens and HIV antibodies simultaneously may allow for detection of HIV in a sample at an earlier stage of infection, thereby closing the diagnostic window slightly and allowing for earlier diagnosis (p. 3, lines 20-27; p. 5, line 33 to p. 6, line 18; p. 6, lines 23-29). Specifically, Schonbrunner teach detecting an analyte (HIV) that has at least two analyte-specific components (HIV antigens including p24 and HIV antibodies) in a sample by simultaneously or sequentially contacting the sample with at

least one first receptor ("antigen capture reagent") and at least two second receptors ("antibody capture reagents") (see p. 6, line 33 to p. 8, line 8) and with a detection reagent that may be specific for the analyte in a non-competitive detection assay format (p. 11, line 4 to p. 14, line 17). The two or more antibody capture reagents would also constitute first and second receptors specific for different analyte-specific components as claimed, since they may be directed against antibodies with different antigenic or epitopic specificity (p. 17, lines 6-8). Schonbrunner also teaches detection of different types, groups, or subgroups of HIV (p. 8), which would also be considered to be different "analyte-specific components".

The detection reagent of Schonbrunner comprises a receptor that binds specifically with the analyte (either the HIV antigens or antibodies) (p. 22, line 11 to p. 23, line 3). The detection reagent further comprises a signal-generating group, which may be conjugated to the receptor before or after complex formation (p. 23, line 4 to p. 25, line 11). In a preferred embodiment the first and second receptors are bound to a solid support (p. 16, lines 14-16; p. 17, lines 9-15; p. 18, lines 10-23), which can be provided together with the detection reagent as part of a kit (p, 35, line 15 to p. 36, line 11).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the solid phase and simultaneous, multiple analyte detection method of Ekins et al. to simultaneously detect HIV antigens and HIV antibodies, as taught by Schonbrunner, in order to diagnose HIV at an earlier stage of infection.

One would have a reasonable expectation of success because Ekins et al. teach that the solid phase may be used to simultaneously detect multiple analytes in a sample, which is the

purpose of the method of Schonbrunner (i.e., to simultaneously detect both HIV antigens and HIV antibodies in a sample).

One would also have a reasonable expectation of success in using the solid phase of Ekins et al. in the method of Schonbrunner because Schonbrunner also teaches that the analyte receptors may be attached to the same or a different solid supports (column 18, lines 10-23) and that the particular type of solid support is not critical (p. 20, lines 9-14). Microtiter plate wells are one example of a suitable solid support in Schonbrunner (column 20, lines 9-22), which is also an embodiment of the solid phase of Ekins.

One would also have a reasonable expectation of success because Ekins et al. teach that the solid phase may be used to detect proteins, which are the analyte-specific components detected in Schonbrunner.

With respect to claim 45, Schonbrunner et al. teach detection of HIV-1 antigens and antibodies (column 8, lines 29-35 in particular).

With respect to claims 46 and 50, the microspots of Ekins et al. have a diameter of 0.01 to 1 mm (column 5, lines 10-17).

With respect to claim 47, Ekins et al. teach that the solid phase may include control areas

With respect to claims 48 and 52, Ekins et al. teach a universal marker reagent such as avidin conjugated to fluorescent microspheres (column 4, lines 40-62; column 15, lines 50-58) and such microspheres may be latex (column 3, lines 58-column 4, line 9).

With respect to claim 73, Schonbrunner teach detection of different analyte-specific antigens (e.g., p17, p24, p2, gp120, gp41) as well as antibodies specific for these different antigens (see in particular p. 7, line 24 to p. 8, line 9).

24. Claims 47 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of Schonbrunner as applied to claim 44 above, and further in view of O'Connor et al. (US 5627,026).

Ekins et al. and Schonbrunner et al. are as discussed above, which teach a solid phase and assay method for multicomponent detection of HIV. However, the references fail to specifically teach that the solid phase includes a control area or that the analyte in the sample is determined via a test area-specific cut-off.

O'Connor et al. teach methods for simultaneously determining an antibody and an antigen in a sample, such as an HIV antibody and an HIV antigen (column 2, lines 27-59). In particular, O'Connor et al. teach that wells of a microtiter plate in an ELISA assay may be used as controls (columns 8-9, "ELISA test for FIV). This is done in order to determine whether the assay is valid (see in particular column 9, lines 17-25). O'Connor et al. further teach when the signal from a test area is 3 times greater than that from the negative control that the presence of the analyte may be positively determined.

Therefore, it would have been obvious to one of ordinary skill in the art to employ control areas as taught by O'Connor et al. in the solid phase of Ekins et al. in performing the method of Ekins et al. and Schonbrunner et al. in order to determine whether the assay was valid. It would have been further obvious to employ a test area-specific cut-off value as taught by O'Connor in order to determine whether a signal from a test area was positive.

25. Claims 46, 48, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linsley et al. in view of Ekins et al. (US 5,516,635).

Linsley et al. is as discussed above, which teaches test areas that are wells of a microtiter plate, but which fails to specifically teach that the test areas have diameters of the recited size.

Linsley et al. teach detection reagents that comprise radionuclides such as ^{125}I or the enzyme HRP (see column 4, lines 11-15), but fail to specifically teach a detection reagent that comprises a signal-generating group that is a universal detection reagent comprising labeled latex particles.

With respect to claims 46 and 50, Ekins et al. (discussed above) teaches solid supports including microtiter plate wells, in which capture binding agents may be deposited as microspots having sizes of 0.01-1 mm in diameter. Ekins et al. teach that the microspots allow for less consumption of a possible scarce and costly reagent (capture antibody) (column 2, lines 7-8) and that by microspotting a small amount of capture binding agent in a small area at high density, greater assay sensitivity may be achieved (column 2, lines 15-60; column 3, lines 6-22).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the microspotted test areas of diameter 0.01-1mm as taught by Ekins et al. in the method and solid phase of Linsley et al. in order to increase assay sensitivity and allow for less consumption of capture antibody. One would have a reasonable expectation of success because Ekins et al. teaches that the microspots may be used in non-competitive assay systems, which describes the sandwich immunoassay of Linsley.

With respect to claims 48 and 52, Ekins et al. teach detection reagents such as avidin conjugated to fluorescent microspheres, which may be latex microspheres (column 3, line 48 to

column 4, line 9; column 4, lines 40-47; and column 15, lines 49-67). Ekins et al. teach that such "universal marker" reagents can bind to all binding materials and point to the advantages of such universal marker reagents. Ekins et al. further teach that the labeled with fluorescent material in order to allow signal amplification, thereby increasing assay sensitivity (column 4, line 63 to column 5, line 9).

Therefore, it would have been further obvious to one of ordinary skill in the art to employ a universal detection reagent comprising latex microspheres as taught by Ekins et al. in the method and test kit of Linsley et al. in order to allow for signal amplification and use of a universal reagent capable of binding to all types of binding materials.

Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 44-52 and 73-74 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,815,217. Although the conflicting claims are not identical, they are not patentably distinct from each other because US 6,815,217 also claims a solid phase comprising a first and second spatially separate test area, which comprise, respectively, first and second receptors (see claims 1 and 17 in particular). The first receptor is specific for a first analyte and the second receptor is specific for a second analyte. The analyte may be HIV antibodies, HBs antigens, and HBc antibodies (claims 18 and 30). The solid phase may also include a control area (see claim 19). The solid phase may be provided together with a third receptor capable of binding to the analyte, which receptor may include a signal generating group (see claims 19 and 34). The solid phase may be used in an assay method to detect an analyte in a sample (claims 19-33).

US 6,815,217 does not specifically recite that the second receptor binds to a different "analyte-specific component" of the analyte than the first receptor; rather, the claims recite that the second receptor specifically binds to a second analyte (see claim 17), one skilled in the art would recognize that the claims overlap in scope because the analytes detected in US 6,815,217 may be HBs antigens and HBc antibodies (see claim 18). Since HBs antigens and HBc antibodies would both be considered to be "analyte-specific components" of the analyte HB (Hepatitis B virus) as a result of the way in which Applicant is employing the terms "analyte" and "analyte-specific components" (as discussed above), one skilled in the art would recognize that HBs antigens and HBc antibodies are species that anticipate the genus of "analyte-specific components" claimed in the instant application.

Furthermore, although US 6,815,217 does not specifically recite that the solid phase comprises a "non-porous" support, it would have been obvious to one skilled in the art to employ the specification as a dictionary in order to interpret the "solid phase support" claimed for guidance in carrying out the claimed invention. In introducing the solid phase support, the specification of US 6,815,217 at column 2, lines 29-32 states that the support is preferably non-porous.

Response to Arguments

28. With respect to the rejections of claims 44, 47, 49, and 51 under 35 USC 102(e) as being anticipated by Linsley et al., Applicant argues that Linsley et al. fails to teach that different analyte-specific receptors are applied onto one solid phase in different test areas, and that only one antibody is immobilized onto a solid phase, e.g. Onc-M26 **or** Onc-M29 as the capture antibody (p. 12-13). Applicant's arguments have been fully considered but they are not persuasive. The use of the wording "Immulon II plates were incubated with 50 µl/well of 10 µg/ml of Onc-M26, or Onc-M29" by Linsley et al. in describing the experiment of Example IV (column 17, lines 57-58) reflects the fact that either Onc-M26 **or** Onc-M29 was added to an individual well, rather than a scenario in which both antibodies were added to the same well. However, Linsley et al. clearly teach that both antibodies were in fact immobilized. See Linsley et al. at column 17, lines 52-56:

> "To demonstrate the usefulness of the monoclonal antibodies described herein, a DDIA was performed using the monoclonal antibodies Onc-M26 **and** Onc-M29..." (emphasis added)

It is also clear that both antibodies were in fact immobilized since data for both Onc-M26 and Onc-M29 are reported in Table 5 (see also Linsley et al. at column 18, lines 1-50).

Conclusion

29. No claims are allowed.

30. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Croxson et al. (US 5,108,891) also teaches the use of controls and cut-off values in diagnostic applications.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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